INOSR Experimental Sciences 13(2):15-22, 2024. ISSN: 2705-1692
©INOSR PUBLICATIONS INOSRES1321522.00
International Network Organization for Scientific Research
https://doi.org/10.59298/INOSRES/2024/1321522.000

Ameliorative potentials of methanol leaf extract of *Anthocleista vogelli* on mercury chloride induced neurotoxicity

[1,3*]Egba, Simeon Ikechukwu; [2]Okonkwo, Chibuzor Onyinye; [3]Kalu, Uguru Grace [3]Paul Promise, [1]Chibuike, Sampson Nzubechi L, [4]Egbachukwu Blessing Ifeoma [1]Alum Esther Ugo and [1]Ugwu Okechukwu Paul-Chima

[1]Department of Biochemistry, Research and Extension, Kampala International University, Uganda
[2]Department of Biochemistry, Faculty of Basic Medical Sciences, University of Calabar, Cross Rivers State, Nigeria.
[3]Department of Biochemistry, Michael Okpara University of Agriculture, Umudike Abia State, Nigeria.
[4]Faculty Veterinary Medicine, University of Nigeria, Nsukka, Nigeria
Corresponding Author:Dr Simeon Ikechukwu Egba; +2348037750598, Simeon.egba@kiu.ac.ug, 0000-0002-8442-8869

ABSTRACT

In this work, the effects of A. vogelli leaf extract on a few neurotoxicity indicators in Wistar rats were examined. Group 1 consisted of a normal control group, Group 2 of mercury (II) chloride, Group 3 of mercury (II) chloride + Diazepam 5 mg/kg, and Group 4 of mercury (II) chloride + plant extract 400 mg/kg bw. The sixteen (16) male rats were divided into these four groups at random. Animals were slaughtered and medications and extracts were administered for 21 days. Cerebellum and cerebrum brain samples were obtained and examined. Using accepted procedures, assays for acetylcholinesterase, alpha-tocopherol, and adenine deaminase were conducted. The acetylcholinesterase activity, vitamin E concentration, and adenine deaminase activity in the untreated groups were significantly ($p \leq 0.05$) higher than in the control group. Additionally, it was noted that both the plant extract and the usual medication, diazepam, showed significantly higher levels of vitamin E and adenine deaminase activity ($p \leq 0.05$) accompanied with lower acetycholinesterase activity. This suggests that the plant extract may have the potential to be a neuroprotective agent and could be used to treat neurotoxicity and other related disorders.

Keywords: Neurotoxicity, acetylcholinesterase, alpha-tocopherol, adenine deaminase, *Anthocleista vogelli.*

INTRODUCTION

Numerous physiologically active substances found in plants have the potential to be developed into therapeutic medicines. Although the industrialised world has also embraced the use of herbal medicines, poor nations still rely heavily on them for medicinal purposes [1,2]. Many plants are said to have medicinal and protective qualities in traditional medicine [3]. Given the abundance of complex secondary metabolites that plants possess, it is expected that they will remain a rich source of novel compounds. There are several medical diseases associated with disruptions in neural function. This is mostly caused by an increase in environmental variables such mercury that cause neurotoxicity [4]. This makes it crucial to look for natural products that may be able to reduce neurotoxicity. The Gentianaceae family currently includes trees and shrub-like plants such as *Anthocleista vogelii*, which is commonly referred to as the "cabbage tree" in English due to some species' unbranched stems or stems that branch only at the top with enormous leaves clustered at the end of the shoot ([5], "sapo" or "apaoro" in Yoruba, "kwari" in Hausa, "orimi" in Benin, "mpoto" in Igbo ([6], and "odogwu" in Igala,

Nigeria. A. vogelii's many therapeutic benefits have brought it international attention in recent years. Traditional medicine has used all components of the *Anthocleista vogelii* tree—leaves, blossoms, seeds, fruits, roots, and bark—to cure fever, infections, inflammation, skin conditions, and dental issues ([7]. The leaves, stem-bark, and root bark of A. vogelii contain significant amounts of phytochemicals [8,9]. The leaf and stem bark of the Anthocleista species were found to be devoid of reducing sugar, tannin, phlobatanins, and glycosides. Segmentoganin, decussatin, swertiaperennin, 1-hydroxy-3,7-dimethoxyxanthone, 7α-hydroxysitosterol, stigmasterol, hexadecanoicacid, sitosterol3-O-β-D-glucopyranoside, fagaramide, andtriterpenes are among the other chemical substances that have been identified from *A. volgelli* [10].The anti-inflammatory, anti-hyperglycemic, anti-ulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic, endocrine modulatory, and anticarcinogenic qualities of *Anthocleista vogelii* Planch leaf and its constituents have been shown [11,12,13]. It is beneficial to use Wistar rats to study the potential neuroprotective impact of methanol extracts from this plant's leaves, given the variety of therapeutic treatments that may be made using it. Neuromodulation capabilities of plant products have been documented [4].

Materials and procedures

The mature plant of *Anthocleista vogelii* was harvested for its leaves in a farm located in Umudike, Abia State. The Department of Plant Science and Biotechnology (PSB) at Michael Okpara University of Agriculture Umudike (MOUAU), in Abia State, Nigeria, has the proper authority to identify the plant sample. A methodical process was followed to get the plant extract: 500g of *A. Vogelli* leaves were first gathered, air dried, and milled into a powder. A precise 100g portion of the powder was immersed in 700 mL of methanol for a whole day. Subsequently, it was extracted and passed through a filter paper filter into a sterile beaker. After the filtrate was totally evaporated, the methanol was concentrated using a water bath at 40–50°C, leaving only the gel-like green extract, which was then refrigerated at 4°C until it was needed.

Animals used in experiments

Male adult Wistar albino rats, weighing around 100–130g, were obtained from the animal unit of Michael Okpara University of Agriculture's College of Veterinary Medicine in Umudike, Abia State, Nigeria. The animals were kept in a well-ventilated environment with a 12-hour light/dark cycle, given standard feed (Vital feeds inc), and allowed unrestricted access to water. Prior to the trial starting, they were housed in aluminium cages and given two weeks to become used to their surroundings. The investigation was conducted in compliance with the Good Laboratory Practice (GLP) guidelines established by the Organisation for Economic and Development (OECD) (OECD). The ethical committee on the use of animals at the College of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike, Nigeria, provided prior ethical permission (Code number: UMSE/06/012). Standard medications and sample were used. Following the evaporation of methanol, the standard pharmaceuticals and *Anthocleista vogelii* aqueous extract were made by immediately weighing and dissolving the known weight of the medicines and solid extract in the necessary amount of de-ionized water and tween 80 initiation of neurotoxicity Each rat was given an oral dose of mercury chloride (4 mg/kg body weight) in distilled water to induce neurotoxicity. Oral water was given to the control group. Neurotoxicity was assessed seven days after induction by looking for symptoms of hair loss and inflammation in the animal's body, especially in the lower jaw.

Design of Experiments

The rats were split into four groups of four rats each at random. Normal rats in Group 1 (normal control) were given just water and food. Group 2 was the positive control, or neurotoxicant control, and was given 4 mg of mercury chloride per kilogramme of body weight. The rats in group 3 were given a dosage of 5 mg/kg body weight of diazepam after being provoked with the neurotoxicant mercury chloride. Group 4 animals were given a 400 mg/kg body weight dose of the plant extract after being rendered neurointoxicated. For 21 days, the treatments were taken orally once a day. Group 2, the untreated neurointoxicated group, was given simply the vehicle, which was distilled water.

Biochemical analysis

By applying Ellman's method [15] Acetylcholinesterase (AChE) activity was determined. Colorimetric analysis was used to measure serum alpha-tocopherol [17] The adenine deamidase was estimated using the Hitachi 705 discrete analyzer (Boehringer-Mannheim, FRG); it was run on an Acta II spectrophotometer (Beckman

Institute, NY, USA) At the end of the study, the experimental animals were mercifully sacrificed.

Statistical analysis Data was presented as means ± standard error of mean (SEM) and translated into bar charts. Statistical analysis was performed using a one way analysis of variance (ANOVA) in statistical package for social sciences (SPSS) for windows version 20.0 (SPSS Inc,Chicago II, USA).

RESULTS

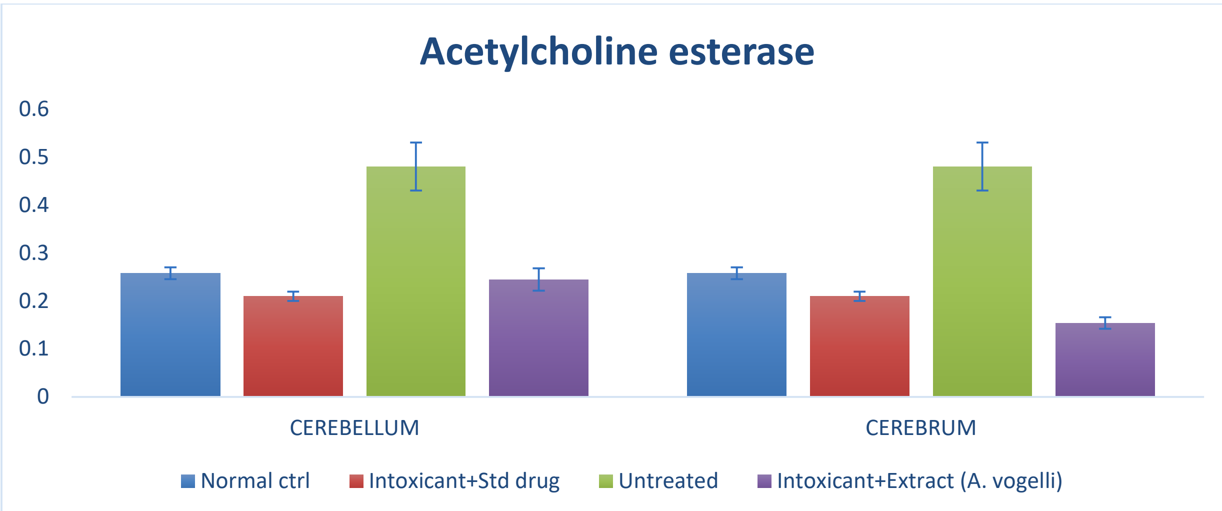

Fig 1: Effect of Methanol Extract of *A. Vogelli* on acetylcholine esterase in the cerebellum and the cerebrum of Wistar albino rat.

Figure 1 significant ($p \leq 0.05$) increase in acetylcholinesterase activity in both the cerebrum and cerebellum of the untreated groups relative to the control group. There was also a significant decrease ($p \leq 0.05$) in AchE activity in the group treated with the standard drug Diazepam.The extract however caused a significant decrease ($p \leq 0.05$) in AchE activity in the cerebrum but not in the cerebellum of treated rats relative to the control.

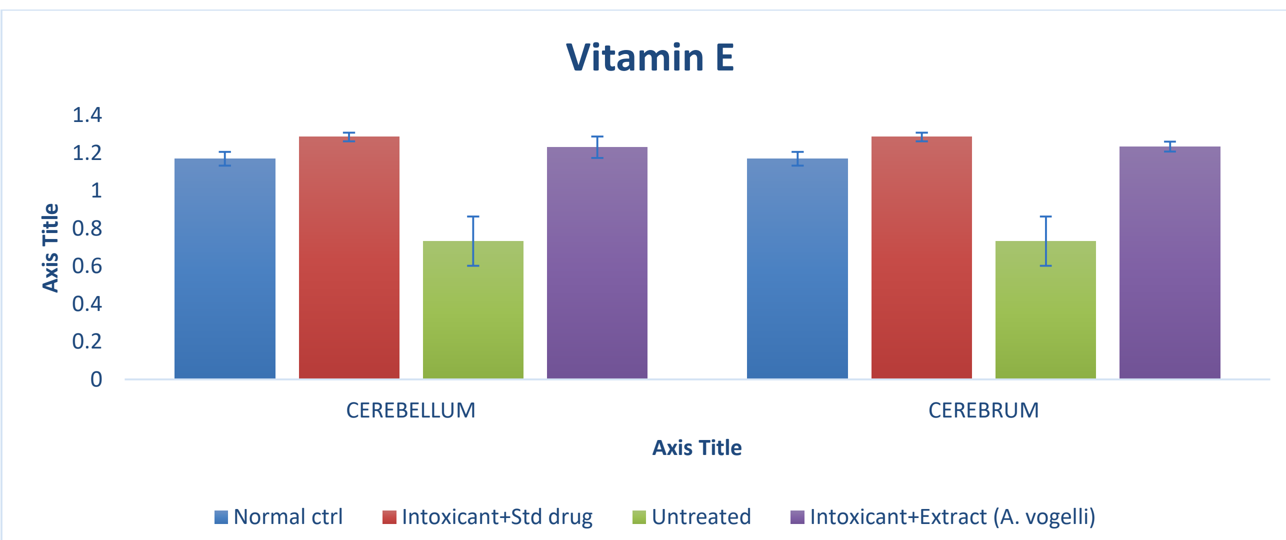

Fig 2: Effect of Methanol Extract of *A. Vogelli* on Vitamin E in the cerebellum and the Cerebrum of Wistar albino rat

Figure 2 showing significant ($p<0.05$) decrease in the concentration of vitamin E in both the cerebellum and cerebrum of the untreated group II relative to the control group I. The standard drug diazepam and the plant extract also caused a significant ($p<0.05$) increase in vitamin E concentration both in the cerebellum and the cerebrum of test animals.

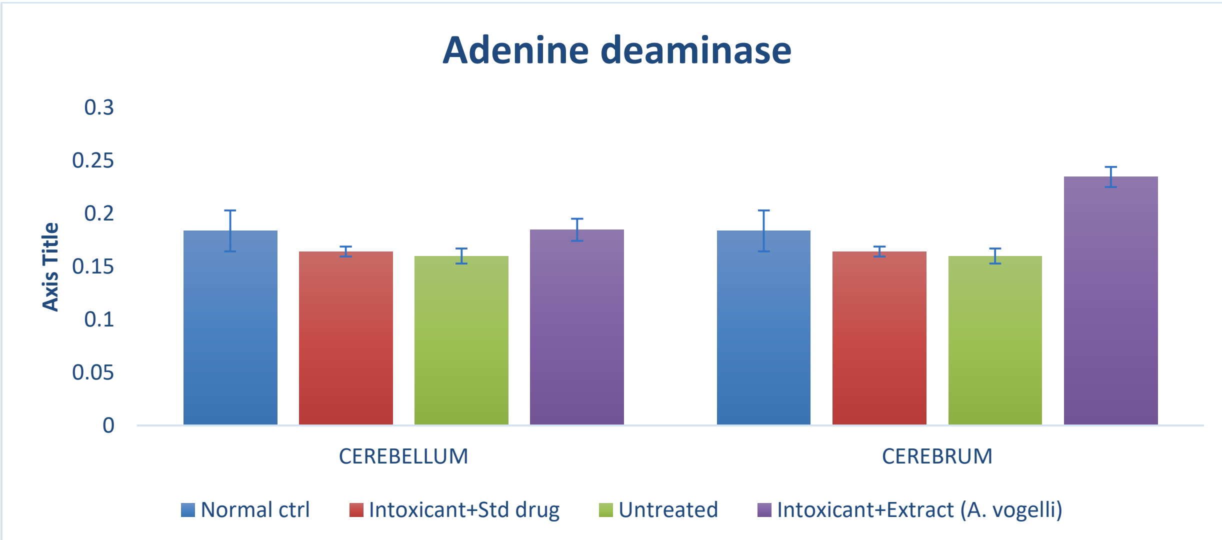

Fig 3: Effect of Methanol Extract of *A. Vogelli* on Adenine deaminase in the cerebellum and the Cerebrum of Wistar albino rat.

Figure 3 showing significant ($p<0.05$) decrease in adenine deaminase activity in the untreated group and the group treated with the standard drug diazepam. The plant extract caused a significant ($p<0.05$) increase in adenine deaminase activity in the cerebrum but not in the cerebellum. While there was significant ($p<0.05$) increase in acetyl cholinesterase activity and decrease in vitamin E concentration and adenine deaminase activity in the untreated groups relative to the normal control.

DISCUSSION

It is possible that mercury (II) chloride caused a deficiency in cholinergic neurotransmission by lowering acetylcholine (Ach) levels at the synaptic cleft, as evidenced by the increase in acetylcholinesterase (AchE) activity seen in the cerebellum and cerebrum of the untreated groups [18]. Low levels of Ach at the synaptic junction may have a deleterious effect on memory, and excess levels of Ach resulting from high AchE activity are also neurotoxic since ACh is a crucial component in the development, maintenance, and evocation of memory processes [19]. The acetylcholine neurotransmitter is hydrolyzed by acetylcholinesterase, which puts a stop to cholinergic neurotransmission. Because of this, it is the main target of a broad range of substances that are used as nerve agents, pesticides, or therapeutic drugs for neurodegenerative diseases like Alzheimer's disease (AD) [20], where inhibition of this enzyme aims to make up for the deficiencies in the cholinergic system that have been linked to AD as well as other illnesses like Parkinson's disease and myasthenia gravis [21]. AChE is involved in neuronal growth in addition to its main function of stopping synaptic transmission. In terms of embryology, AChE is expressed by growing neurons and during axonal growth, and it plays a crucial role in the nervous system's development. By reducing AchE activity, *A. vogelli* extract and diazepam were able to counteract the effects of mercury (II) chloride, a neurotoxic. This suggests that *A.vogelli* may be investigated as a possible therapy option for Alzheimer's disease and other neurodegenerative illnesses. Acetylcholinesterase (AChE) inhibitors have dominated treatment of Alzheimer's disease, a common condition affecting cognition and memory. Through the inhibition of acetylcholine (ACh) turnover and restoration of synaptic levels of this neurotransmitter, these medications compensate for the loss of cholinergic neurons and provide symptomatic relief [22]. Acetylcholine is less broken down and therefore accumulates when AChE is inhibited. There is some treatment relief for the memory problems associated with AD due to the

increased activation of muscarinic and nicotinic receptors caused by this excess acetylcholine [23]. Adenosine deaminase (ADA) is an enzyme that is widely expressed and present in many tissues and fluids. It facilitates the conversion of adenosine into inosine and deoxyadenosine into deoxyinosine, and it is involved in the metabolism of purines and pyrimidines [24]. One of the important enzymes in purine metabolism is thought to be ADA [25]. Neurotransmission, gestation maintenance, and epithelial cell differentiation have all been linked to it [26]. Additionally, it has been suggested that ADA is required for the coupling of ADA1 adenosine receptors with heterotrimeric G proteins, and that it increases the release of excitatory amino acids in addition to breaking down adenosine [27]. The reduction in adenine deaminase activity seen in both the untreated and treated groups with normal diazepam suggests that mercury (II) choride and diazepam may have induced hypogammaglobulinemia, which in turn may have produced immunodeficiency of the brain cell. According to reports, ADA deficiency may result in a number of abnormalities, such as cytopenias, immunodeficiency brought on by hypogammaglobulinemia, and vasculitis, Behçet's-like illness [28, 29, 30]. Pulmonary fibrosis might potentially result from decreased adenosine deaminase activity [31]. By raising adenine deaminase activity in the cerebrum but not the cerebellum, *A. Vogelli* was able to counteract the harmful effects of mercury II choride. Remarkably, diezepam, a typical medication, was unable to undo this impact. This implies that the extract from *A. volgelli* might be a promising option for immunomodulatory medications. The standard drug diazepam and the plant extract were able to reverse this effect by causing a significant ($p<0.05$) increase in vitamin E concentration in both the cerebellum and the cerebrum of test animals. The untreated group showed a significant ($p<0.05$) decrease in vitamin E concentration in both the cerebellum and the cerebrum compared to the control group. The term "vitamin E" refers to a class of fat-soluble substances having unique antioxidant properties [32]. The only tocopherol recognised to suit human needs is alpha (α-) tocopherol. The hepatic alpha-tocopherol transfer protein allows the liver to selectively re-secrete just alpha-tocopherol [33]. The majority of the time, diseases such as Crohn's disease, liver disease, cystic fibrosis, and some uncommon genetic abnormalities are to blame for vitamin E insufficiency because they impair the body's ability to digest or absorb nutrients [34]. This suggests that, potentially via fat-malabsorption, mercury II chloride may have interfered with the test animals' ability to digest and absorb vitamin E. People with illnesses related to fat-malabsorption are also more prone to become deficient in vitamin E than those without such problems since the digestive system needs fat to absorb the vitamin. Peripheral neuropathy, ataxia, skeletal myopathy, retinopathy, and immune response impairment are examples of deficiency symptoms [35]. Lack of vitamin E as a result of abetalipoproteinemia may result in blindness due to retinal degeneration, weak muscles, and impaired nerve impulse transmission [36]. The potential of vitamin E to improve health and both prevent and cure illness has been the subject of several claims. Vitamin E is the most significant lipophilic antioxidant and is mostly found in cellular membranes, where it contributes to membrane integrity [37]. Antioxidants shield cells from the cellular damage caused by free radicals, which have the potential to cause cancer and cardiovascular disease [38]. Reactive oxygen species are created when extremely energetic unshared electrons quickly react with oxygen (ROS). The environment, including cigarette smoke, air pollution, and UV radiation from the sun, exposes the body to free radicals. Being a fat-soluble antioxidant, vitamin E prevents the oxidation of fat from producing reactive oxygen species (ROS). Immune system performance, cell signalling, gene expression regulation, and other metabolic processes are all impacted by vitamin E [39] Protein kinase C, an enzyme involved in smooth muscle cell, platelet, and monocyte proliferation and differentiation, is inhibited by alpha-tocopherol [32]. Endothelial cells rich in vitamin E that line the inside of blood arteries are more resilient to blood cell components sticking to their surface. Additionally, vitamin E enhances the production of two enzymes that restrict the metabolism of arachidonic acid, boosting the endothelium's release of prostacyclin, which dilates blood vessels and prevents platelet aggregation [35]. The neuronal cell membranes of the brain contain a large amount of polyunsaturated fatty acids and have a high oxygen consumption rate. Ingestion of enough or additional antioxidants (such as vitamin E) may provide some protection if cumulative free-radical damage to neurons over time leads to cognitive decline and neurodegenerative disorders, such as Alzheimer's disease [39]. A prospective cohort study of older, independent persons aged 65-102 years revealed a correlation between reduced cognitive deterioration over a 3-year period and the usage of vitamin E via foods or supplements [40]. The plant extract may have strong neuroprotective and immunoenhancing properties that should be extracted and used in the

treatment of immunological and neurodegenerative diseases, as evidenced by its ability to reverse the effects of mercury (ii) chloride by reducing acetylcholinesterase activity and increasing vitamin E concentration and adenine deaminase activity.

REFERENCES

[1] De, F. H. and Ifeoma, C. C. W."Respiratory Function of Hemoglobin".New England Journal of Medicine. 2002; 338 (4): 239–247

[2] El-Mahmood, T.Y., Erich, K.C and Sackmann, Y.U. "Biological Membranes Architecture and Function; Handbook of Biological Physics, (ed. R.Lipowsky and E.Sackmann, vol.1, Elsevier). 2010

[3] Kayode,. A. O and Kayode. B.O. Nutritional potentials of some tropical vegetable leaf meals: chemical characterization functional properties. African Journal of Biotehnology2006; .20(1):97–98.

[4] Egba SI, Famurewa AC, Omoruyi LE. Buchholzia coriacea seed extract attenuates mercury-induced cerebral and cerebellar oxidative neurotoxicity via NO signaling and suppression of oxidative stress, adenosine deaminase and acetylcholinesterase activities in rats. Avicenna J Phytomed. 2022 Jan-Feb;12(1):42-53. doi: 10.22038/AJP.2021.18262.

[5] Keay, A.R.A. The haematological effect of Telfairia occidentalisdiet preparation: African Jounal of Biomedication 2000; 2(1):297–307.

[6] Anyanwu, G.O., Onyeneke, E.C., Usunobun, U., Adegbegi, AJ Impact of Anthocleista vogelii root bark ethanolic extract on weight reduction in high carbohydrate diet induced obesity in male wistar rats. Afr. J. Biochem. Res. 2013; 7:225-232.

[7] Anyanwu, G.O., Rehman , N., Onyeneke, C. E ., Rauf, K. Medicinal plants of the genus Anthocleista--A review of their ethnobotany, phytochemistry. and pharmacology. J Ethnopharmacol 2015; 4; 175:648-67.doi: 10.1016/j.jep.2015.09.032.

[8] Gboeloh, L.B., Okon, O.E., Udoh, S.E (2014). Antiplasmodial Effect of Anthocleista vogelii on Albino Mice Experimentally Infected with Plasmodium berghei (NK 65) .Journal of Parasitology Research, 2014; 2014, 731906,6 pages,.https//doi.org/10.1155/2014/731906.

[9] Ngbolua, K.N., Mpianab, P.T., Mudogob, V., Ngombec, N.K., Tshibangub, D.S.T., Ekutsua, C.L., Kabenaa, O.N., Gboloa, B.Z., Muanyishaya, C.L. Ethnopharmacological survey and floristical study of some medicinal plants traditionally used to treat infectious and parasitic pathologies in the Democratic Republic of Congo. International journal of Medicinal Plants. 2014; 106; 454–467.

[10] Alaribe, C.S.A., Coker, H.A.B., Shode, F.O., Ayoola, G., Adesegun, S.A., Bamiro, J ., Anyim, E.I., Anyakora, C. Antiplasmodial and phytochemical investigations of leaf extract of Anthocleista vogelii (Planch) National Journal 2012; 5; 60–67.

[11] Subapriya, L. V. and Nagini J. A. Vaginitis: current microbiologic and clinical concepts Clinical journal 2005; 20; 15-46.

[12] Eze , F.I., Noundou, X.S., Osadebe, P.O and Krause, R.W.M. Phytochemical, anti-inflammatory and anti-trypanosomal properties of Anthocleista vogelii Planch (Loganiaceae) stem bark. J Ethnopharmacol. 2019; 28;238:111851. doi: 10.1016/j.jep.2019.111851.

[13] Egba, Simeon I., Okonkwo Chibuzo O, Omeoga Humphrey C and Ekong I E. Comparative modulation of the reproductive system by ethanol leaf extracts of Asystasia gangetica and Anthocleista vogelii in male Wistar rats. European Journal of Medical and Health Sciences. 2020; 2(3): 387-392

[15] Ellman G. L., Courtney K. D., Andres V. Jr., and Featherstone R. M. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem. Pharmacol. 1961; 7, 88-95

[17] Jargar , J.G., Hattiwale, S.H., Das, S., Dhundasi, S.A., Das, K.K. A modified simple method for determination of serum α-tocopherol (vitamin E). J Basic Clin Physiol Pharmacol, 2012; 19; 23(1):45-8. doi: 10.1515/jbcpp-2011-0033.

[18] Mitchell, G.A., Grompe, M., Lambert, M., Tanguay, R.M. Hypertyrosinemia In: Scriver, C.R., Beaudet, A.L. Sly, W.S., Valle, D. (8th Ed). The Metabolic and Molecular Bases of Inherited Disease, McGraw-Hill, New York, 2001; pp. 1977-1982.

[19] Soreq, H and Seidman, S Acetylcholinesterase – new roles for an old actor. Nat. Rev. Neurosci. 2001; 2, 294-302.

[20] Rienda, B., Elexpe, A., Tolentino-Cortez, T., Gulak, M., Bruzos-Cidón, C., Torrecilla, M., Astigarraga, E., Barreda-Gómez, G. Analysis of Acetylcholinesterase Activity in Cell Membrane Microarrays of Brain Areas as a Screening Tool to Identify Tissue Specific Inhibitors. Analytica, 2021 2, 25–36. https://doi.org/10.3390/ analytica2010003.

[21] Pohanka, M. Cholinesterases, a target of pharmacology and toxicology. Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub, 2011; 155, 219–229.

[22] Rees, T.M., Brimijoin, S. The role of acetylcholinesterase in the pathogenesis of Alzheimer's disease. Drugs Today (Barc)2003; 39 (1):75-83. doi: 10.1358/dot.2003.39.1.740206.

[23] Lazarevic-Pasti, T., Leskovac, A., Momic ,T., Petrovic , S., Vasic, V. Modulators of Acetylcholinesterase Activity: From Alzheimer's Disease to Anti-Cancer Drugs. Curr Med Chem 2017; 24(30):3283-3309. doi: 10.2174/0929867324666170705123509.
[24] Contreras-Aguilar M.D., Tvarijonaviciute A., Monkeviciene I., Martín-Cuervo M., González-Arostegui L.G., Franco-Martínez, L., Cerón, J.J., Tecles, F., Escribano, D. Characterization of total adenosine deaminase activity (ADA) and its isoenzymes in saliva and serum in health and inflammatory conditions in four different species: an analytical and clinical validation pilot study. BMC Vet Res. 202; 12; 16 (1):384. doi: 10.1186/s12917-020-02574-2.
[25] Losey, H.C., Ruthenburg, A.J., Verdine, G.L. "Crystal structure of Staphylococcus aureus tRNA adenosine deaminase TadA in complex with RNA". Nature Structural & Molecular Biology 2006; 13 (2): 153–159. doi:10.1038/nsmb1047.
[26] Moriwaki Y., Yamamoto, T., Higashino, K. "Enzymes involved in purine metabolism--a review of histochemical localization and functional implications". Histology and Histopathology. 1999; 14 (4): 1321–1340.
[27] Cristalli G, Costanzi S, Lambertucci C, Lupidi G, Vittori S, Volpini R, Camaioni E (2001). "Adenosine deaminase: functional implications and different classes of inhibitors". Medicinal Research Reviews.2001; 21 (2): 105–128. doi:10.1002/1098-1128(200103)21:2<105.
[28] van Well GTJ, Kant B, van Nistelrooij A, Sirma Ekmekci S, Henriet SV, Hoppenreijs E, et al. Phenotypic variability including Behçet's disease-like manifestations in DADA2 patients due to a homozygous c.973-2A>G splice site mutation. Clin Exp Rheumatol. 2019; 37 (Suppl 121):142–6.
[29] Meyts I, Aksentijevich I. Deficiency of adenosine Deaminase 2 (DADA2): updates on the phenotype, genetics, pathogenesis, and treatment. J Clin Immunol. 2018; 38:569-78
[30] Blackburn, M.R (2003). "Too much of a good thing: adenosine overload in adenosine-deaminase-deficient mice". Trends in Pharmacological Sciences. 2003; 24 (2): 66–70. doi: 10.1016/S0165-6147(02)00045-7.
[31] Burnstock G. Purinergic. Signalling-an overview. Novartis Found Symp 2006; 276:26–48 discussion 48–57, 275–81.
[32] Traber, M.G. Vitamin E. In: Shils ME, Shike M, Ross AC, Caballero B, Cousins R, eds. Modern Nutrition in Health and Disease. 10th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2006; 396-411.
[33] Traber, M.G. Vitamin E regulatory mechanisms. Annu Rev Nutr 2007; 27:347-62.
[34] Dietrich M., Traber, M.G., Jacques, P.F., Cross, C.E., Hu, Y., Block, G. Does γ-tocopherol play a role in the primary prevention of heart disease and cancer? A review. Am J Coll Nutr 2006; 25: 292-9.
[35] Institute of Medicine Food and Nutrition Board. Dietary Reference Intakes: Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington, DC: National Academy Press. 2000
[36] Tanyel, M.C., Mancano, L.D. Neurologic findings in vitamin E deficiency. Am Fam Physician; 1997; 55:197-201.
[37] Ozden, S., Catalgol, B., Gezginci-Oktayoglu, S., Arda-Pirincci, P., Bolkent, S., Alpertunga, B. Methiocarb-induced oxidative damage following subacute exposure and the protective effects of vitamin E and taurine in rats. Food Chem. Toxicol.,2009; 47: 1676-1684.
[38] Verhagen, H., Buijsse, B., Jansen, E., Bueno-de-Mesquita, B. The state of antioxidant affairs. Nutr Today 2006;41:244-50.
[39] Sano, M., Ernesto, C., Thomas, R.G., Klauber, M.R., Schafer, K., Grundman, M, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzehimer's disease. N Engl J Med; 1997; 336:1216-22.
[40] Morris, M.C., Evand, D.A., Bienias, J.L., Tangney, C.C., Wilson, R.S. Vitamin E and cognitive decline in older persons. Arch Neurol; 2002; 59:1125-32.

CITE AS: Egba, Simeon Ikechukwu; Okonkwo, Chibuzor Onyinye; Kalu, Uguru Grace Paul Promise, Chibuike, Sampson Nzubechi L, Egbachukwu Blessing Ifeoma, Alum Esther Ugo and Ugwu Okechukwu Paul-Chima (2024). Ameliorative potentials of methanol leaf extract of *Anthocleista vogelli* on mercury chloride induced neurotoxicity. INOSR Experimental Sciences 13(2):15-22. https://doi.org/10.59298/INOSRES/2024/1321522.000